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L7                STR
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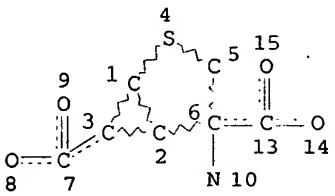


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  13

STEREO ATTRIBUTES: NONE
L9            64 SEA FILE=REGISTRY SSS FUL L7

100.0% PROCESSED      85 ITERATIONS                          64 ANSWERS
SEARCH TIME: 00.00.01


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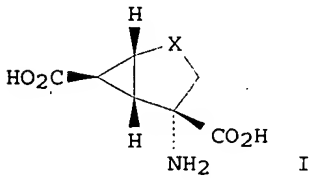
FILE COVERS 1907 - 22 Mar 2007 VOL 146 ISS 13
FILE LAST UPDATED: 21 Mar 2007 (20070321/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs fhitstr hitrn l19 tot

L19 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1341533 HCAPLUS
DN 146:251680
TI Synthesis and Metabotropic Glutamate Receptor Activity of S-Oxidized Variants of (-)-4-Amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylate: Identification of Potent, Selective, and Orally Bioavailable Agonists for mGlu2/3 Receptors
AU **Monn, James A.**; Massey, Steven M.; Valli, Matthew J.; Henry, Steven S.; Stephenson, Gregory A.; Bures, Mark; Herin, Marc; Catlow, John; Giera, Deborah; Wright, Rebecca A.; Johnson, Bryan G.; Andis, Sherri L.; Kingston, Ann; Schoepp, Darryle D.
CS Discovery Chemistry and Neuroscience Research Divisions, **Eli Lilly** and Company, Indianapolis, IN, 46285, USA
SO Journal of Medicinal Chemistry (2007), 50(2), 233-240
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI



I

AB (-)-4-Amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylate (-)-I (X = S) (LY389795) is a highly potent and selective agonist of metabotropic glutamate receptors 2 (mGlu2) and 3 (mGlu3). As part of the ongoing research program, S-oxidized variants of this compound, namely both S-stereoisomers of I (X = SO) and I (X = SO2), were synthesized. Each of these chiral heterobicyclic amino acids displaced specific binding of the mGlu2/3 receptor antagonist 3H-2S-2-amino-2-(1S,2S-2-carboxycycloprop-1-yl)-3-(xanth-9-yl)propanoic acid (3H-LY341495) from membranes expressing recombinant human mGlu2 or mGlu3 and acted as potent agonists in cells expressing these receptor subtypes. Docking of the most potent of these derivs., (SR)-(+)-I [X = SO, (II)] to mGlu2 revealed the possibility of an addnl. H-bond interaction between the sulfoxide oxygen of II with tyrosine residue Y236. Pharmacokinetic anal. of mGlu active enantiomers II and (-)-I (X = SO2) in rats showed each to be well absorbed following oral administration. Consistent with their mGlu2/3 agonist potency and pharmacokinetic properties, both II and (-)-I (X = SO2) blocked

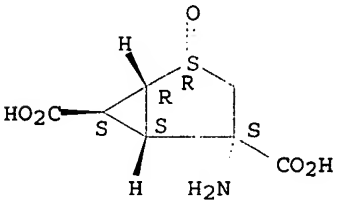
phencyclidine-evoked ambulations in a dose-dependent manner, indicating their potential as nonclassical antipsychotic agents.

IT **926291-20-5P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(crystal structure and mol. modeling; synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as orally bioavailable agonists for mGlu2/3 receptors)

RN 926291-20-5 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, 2-oxide, (1R,2R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **926291-20-5P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(crystal structure and mol. modeling; synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as orally bioavailable agonists for mGlu2/3 receptors)

IT **926291-16-9P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(crystal structure; synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)

IT **926291-14-7**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL (Biological study)
(synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)

IT **635318-11-5P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)

IT **222529-89-7**
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)

IT **926291-19-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and metabotropic glutamate receptor activity of S-oxidized

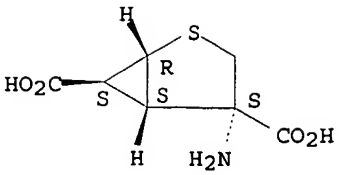
derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)

IT **635317-62-3P 926291-15-8P 926291-17-0P 926291-18-1P 926291-21-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:761719 HCAPLUS
DN 143:279124
TI Analgesic effects of the selective group II (mGlu2/3) metabotropic glutamate receptor agonists LY379268 and LY389795 in persistent and inflammatory pain models after acute and repeated dosing
AU Jones, Carrie K.; Eberle, Elizabeth Lutz; Peters, Stephen C.; **Monn, James A.**; Shannon, Harlan E.
CS **Lilly** Research Laboratories, **Eli Lilly** and Company, Indianapolis, IN, 46285, USA
SO Neuropharmacology (2005), 49(Suppl. 1), 206-218
CODEN: NEPHBW; ISSN: 0028-3908
PB Elsevier B.V.
DT Journal
LA English
AB Group II (mGluR2/3) metabotropic glutamate receptors have been implicated in the mechanisms of persistent pain states. In the present study, the effects of the selective group II metabotropic glutamate receptor agonists LY379268 and LY389795 were evaluated in the formalin test, carrageenan-induced thermal hyperalgesia and mech. allodynia, and capsaicin-induced mech. allodynia in rats. The agonists LY379268 and LY389795 produced dose-dependent decreases in formalin-induced behaviors that were antagonized by the mGlu2/3 receptor antagonist LY341495. The group II antagonist LY341495 produced parallel shifts in the LY379268 dose-response curve, consistent with a competitive antagonism. LY379268 decreased formalin-induced behaviors after intracisternal but not intrathecal administration, suggesting primarily a supraspinal site of action. Both LY379268 and LY389795 produced a dose-related reversal of carrageenan-induced thermal hyperalgesia and capsaicin-induced mech. allodynia, but had no effect on carrageenan-induced mech. allodynia. Both agonists also increased response latencies in the hot plate test, but were without effect in the tail-flick test. However, both agonists produced motor impairment on the inverted screen at doses that were analgesic. Moreover, tolerance to the analgesic effects of LY379268 developed after 4 days of once-daily repeated administration in the formalin, carrageenan, capsaicin and hot plate tests. The present findings indicate that group II (mGluR2/3) metabotropic glutamate receptors may be involved in the mechanisms of hyperalgesia and allodynia, however tolerance rapidly develops to these effects.
IT **222529-89-7**, LY389795
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesic effects of LY379268 and LY389795 in persistent and inflammatory pain models)
RN 222529-89-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-(9CI) (CA INDEX NAME)

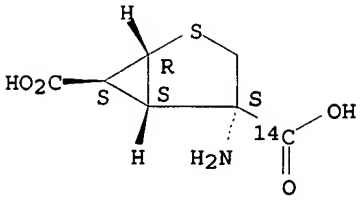
Absolute stereochemistry. Rotation (-).



IT **222529-89-7**, LY389795
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesic effects of LY379268 and LY389795 in persistent and inflammatory pain models)
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:714957 HCAPLUS
DN 144:274498
TI The synthesis of isotopically labeled (+)-2-aminobicyclo[3.1.0]hexane-2,6-carboxylic acid and its 2-oxa- and 2-thia-analogs
AU Wheeler, William J.; O'Bannon, Douglas D.; Kennedy, Joseph H.; **Monn, James A.**; Tharp-Taylor, Roger W.; Valli, Matthew J.; Kuo, Fengjiun
CS **Lilly** Research Laboratories, A Division of **Eli Lilly** and Company, Indianapolis, IN, 46285, USA
SO Journal of Labelled Compounds & Radiopharmaceuticals (2005), 48(8), 605-620
CODEN: JLCRD4; ISSN: 0362-4803
PB John Wiley & Sons Ltd.
DT Journal
LA English
AB As part of a program aimed at the design of conformationally constrained analogs of glutamic acid, (+)-2-aminobicyclo[3.1.0]hexane-2,6-carboxylic acid (I), identified as a highly potent, selective, group II metabotropic glutamate receptor agonist was synthesized and studied clin. Heterocyclic analogs of I were subsequently synthesized in which the C(2) methylene was replaced by an oxygen atom (II) or a sulfur atom (III). Carbon-14-labeled isotopomers of I-III were synthesized to facilitate pre-clin. ADME studies. A tritium-labeled isotopomer of I was also synthesized for use in in vitro expts. A stable labeled isotopomer of rac-I was prepared for use as an internal standard for bioanal. assays. The key step in each of these syntheses was the reaction of 2-oxobicyclo[3.1.0]hexane-6-carboxylic acid (IV) or the appropriate aza or thia compound with K14CN/(NH4)2CO3 using the Bucherer-Berg protocol. In the preparation of the stable labeled isotopomer, rac-IV-[13C2] was prepared in two steps from Et bromoacetate-[UL-13C2]. Subsequent reaction of rac-IV-[13C2] with K13CN/15NH4Cl/Na2CO3, followed by hydrolysis of the hydantoin yielded rac-I-[13C3,15N].
IT **878283-10-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of isotopically labeled aminobicyclo[3.1.0]hexanecarboxylate and oxa and thia analogs)
RN 878283-10-4 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic-4-14C acid, 4-amino-, (1R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **878283-10-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of isotopically labeled aminobicyclo[3.1.0]hexanecarboxylate and oxa and thia analogs)
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:991499 HCAPLUS
DN 140:42463
TI Preparation of prodrugs of excitatory amino acids
IN **Moher, Eric David; Monn, James Allen;**
Pedregal-Tercero, Concepcion
PA **Eli Lilly** and Company, USA; Collado, Cano Ivan;
Blanco-Urgoiti, Jamie Gonzalo
SO PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

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PRAI	2002EP-0380120	A	20020611 <--		
	2002EP-0380121	A	20020611 <--		
	2002US-415936P	P	20021003 <--		
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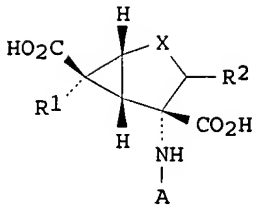
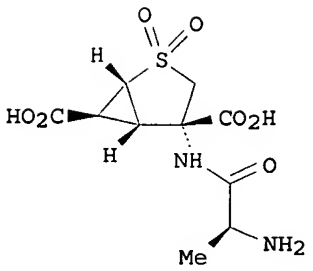
	2003WO-US15405	W	20030606 <--		

OS MARPAT 140:42463
GI



I



II

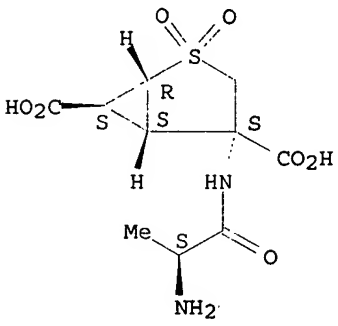
AB The invention relates to synthetic excitatory amino acid prodrugs for the treatment of neurol. disorders and psychiatric disorders. Bicyclic amino acids I [A is H-Q1-10, where Q is aminoacyl; X is O, S, SO, SO2, or substituted methylene; R1 is H or F; R2 is H, F, or OH] or their pharmaceutically-acceptable salts are claimed. Thus, prodrug II.HCl was prepared via peptide coupling reaction and shown to exhibit comparable concentration in rat plasma to that of the non-prodrug form.

IT **635318-22-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of excitatory amino acids)

RN 635318-22-8 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-1-oxopropyl]amino]-, 2,2-dioxide, monohydrochloride, (1R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IT **635318-22-8P 635318-23-9P 635318-24-0P**
635318-25-1P 635318-26-2P 635318-27-3P
635318-28-4P 635318-29-5P 635318-30-8P
635318-31-9P 635318-32-0P 635318-33-1P
635318-34-2P 635318-55-7P 635318-56-8P
635318-57-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of excitatory amino acids)

IT **635317-59-8P 635317-60-1P 635317-61-2P**
635317-62-3P 635317-63-4P 635317-64-5P
635317-65-6P 635317-66-7P 635317-67-8P

635317-68-9P 635317-69-0P 635317-70-3P
635317-71-4P 635317-72-5P 635317-73-6P
635318-06-8P 635318-07-9P 635318-11-5P
635318-67-1P 635702-50-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of prodrugs of excitatory amino acids)

L19 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:818322 HCAPLUS
DN 139:302068
TI Therapy for psychoses combining an atypical antipsychotic and an mGlu2/3 receptor agonist
IN Johnson, Bryan Glenn; Schoepp, Darryle Darwin
PA **Eli Lilly** and Company, USA
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	AU2003218063	A1	20031020	2003AU-0218063	20030321
	EP---1492595	A1	20050105	2003EP-0714045	20030321
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
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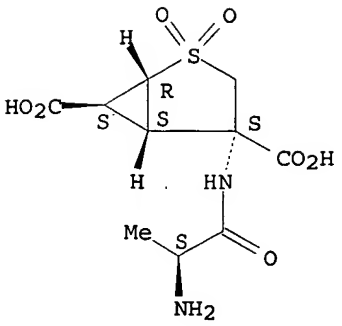
	US2005192273	A1	20050901	2004US-0509772	20040928
PRAI	2002US-369771P	P	20020403		
	2002US-369797P	P	20020403		
	2003WO-US07283	W	20030321		

AB The invention provides a pharmaceutical composition and methods for treating psychosis comprising the combination or a first component which is an atypical antipsychotic with a second component which is a mGlu2/3 receptor agonist. The invention also provides a pharmaceutical composition and method of treating a psychiatric disorder comprising the combination of a first component which is an atypical antipsychotic with a second component which is a compound which allosterically enhances receptor activity for mGlu2 and/or mGlu3.
IT **611168-14-0**, LY 404039
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(atypical antipsychotic-mGlu2/3 receptor agonist combination for treatment of psychoses and psychiatric disorders)
RN 611168-14-0 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-1-oxopropyl]amino]-, 2,2-dioxide, (1R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **611168-14-0**, LY 404039 **611168-15-1** **611168-20-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(atypical antipsychotic-mGlu2/3 receptor agonist combination for treatment of psychoses and psychiatric disorders)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:769630 HCAPLUS
DN 140:246751
TI Comparison of the effect of glutamate receptor modulators in the 6 Hz and maximal electroshock seizure models
AU Barton, Matthew E.; Peters, Steven C.; Shannon, Harlan E.
CS **Lilly** Research Laboratories, Neuroscience Research Division, **Eli Lilly** and Company, Indianapolis, IN, 46285, USA
SO Epilepsy Research (2003), 56(1), 17-26
CODEN: EPIRE8; ISSN: 0920-1211
PB Elsevier Science B.V.
DT Journal
LA English
AB Glutamatergic ionotropic and metabotropic receptor modulators have been shown to produce anticonvulsant activity in a number of animal seizure models, e.g. maximal electroshock (MES) and DBA/2 sensory-induced seizures. The 6 Hz model of partial seizures is an alternative low frequency, long duration stimulation paradigm resulting in a seizure characterized by jaw and forelimb clonus, immobility, and an elevated tail (Straub-tail). A unique aspect of this model is that it is the only acute elec.-induced seizure model in which levetiracetam has displayed anticonvulsant activity, suggesting that the 6 Hz seizure model may be useful in identifying compds. with unique anticonvulsant profiles. The purpose of the present study was to examine the role of glutamate receptors in the MES and 6 Hz seizure models using a number of NMDA, AMPA/KA, and mGlu receptor modulators. The pharmacol. profile of the 6 Hz seizure model was compared to that of the MES model using eight ionotropic glutamate receptor antagonists and eight mGlu receptor modulators. The ionotropic receptor antagonists MK-801, LY235959, NBQX, LY293558, GYKI 52466, LY300168, and LY377770 produced complete protection from tonic extension in the MES model. Furthermore, the noncompetitive mGlu1 (LY456236) and mGlu5 (MPEP) metabotropic receptor antagonists and the mGlu8 metabotropic receptor agonist (PPG) were also effective in the MES model whereas the competitive mGlu1 (LY367385) receptor antagonist, the mGlu2/3 (LY379268 and LY389795) and Group III (l-AP4) metabotropic receptor agonists were ineffective. In contrast, all of the compds. tested, produced dose-dependent protection in the 6 Hz model with an increase in potency as compared to the MES model. The largest protective indexes (P.I.=TD50/ED50) observed were associated with the iGlu5 antagonist LY382884 and the mGlu2/3 receptor agonists LY379268 and LY389795 (P.I.=>14, 14, and 4.9, resp.) in the 6 Hz model. The results from the present study support the continued search for glutamate receptor

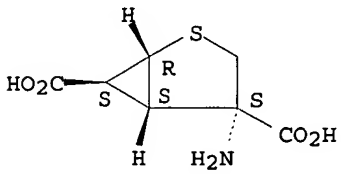
modulators as potential antiepileptic agents. Furthermore these results illustrate the importance of using several different animal seizure models in the search for novel AEDs and the potential utility of the 6 Hz seizure model in identifying novel AEDs.

IT **222529-89-7**, LY389795
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of effect of glutamate receptor modulators in 6 Hz and maximal electroshock seizure models)

RN 222529-89-7 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **222529-89-7**, LY389795
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of effect of glutamate receptor modulators in 6 Hz and maximal electroshock seizure models)

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:531823 HCAPLUS

DN 137:232888

TI (2S,1'S,2'S,3'R)-2-(2'-Carboxy-3'-methylcyclopropyl)Glycine Is a Potent and Selective Metabotropic Group 2 Receptor Agonist with Anxiolytic Properties

AU Collado, Ivan; **Pedregal, Concepcion**; Mazon, Angel; Felix Espinosa, Juan; Blanco-Urgoiti, Jaime; Schoepp, Darryle D.; Wright, Rebecca A.; Johnson, Bryan G.; Kingston, Ann E.

CS **Lilly** SA, Madrid, 28108, Spain

SO Journal of Medicinal Chemistry (2002), 45(17), 3619-3629
CODEN: JMCMAR; ISSN: 0022-2623

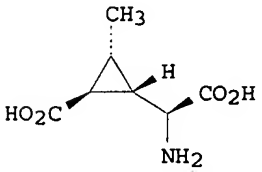
PB American Chemical Society

DT Journal

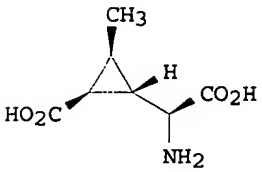
LA English

OS CASREACT 137:232888

GI



I



II

AB The asym. synthesis and biol. activity of (2S,1'S,2'S,3'R)-2-(2'-carboxy-3'-methylcyclopropyl)glycine I and its epimer II (at the C3' center) are described. I is a highly potent and selective agonist for group 2 metabotropic glutamate receptors (mGluRs). It is also systemically 4 orders of magnitude more active in the fear-potentiated startle model of

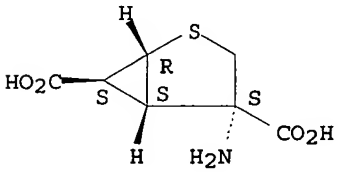
anxiety in rats than the rigid constrained bicyclic system LY354740. In summary, the authors have shown that high mol. complexity of conformationally constrained bicyclic systems is not a requirement to achieve highly selective and potent group 2 mGluRs agonists.

IT **222529-89-7**, LY 389795
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biol. activity comparisons of [(carboxy)(methyl)cyclopropyl]glycine with other selective agonists of metabotropic glutamate receptors)

RN 222529-89-7 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **222529-89-7**, LY 389795
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biol. activity comparisons of [(carboxy)(methyl)cyclopropyl]glycine with other selective agonists of metabotropic glutamate receptors)

RE.CNT 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:512140 HCAPLUS

DN 138:198422

TI Group II mGluR receptor agonists are effective in persistent and neuropathic pain models in rats

AU Simmons, Rosa Maria A.; Webster, Amy A.; Kalra, Anshu B.; Iyengar, Smriti

CS **Eli Lilly** and Company, **Lilly** Research Laboratories, **Lilly** Corporate Center, Indianapolis, IN, 46285, USA

SO Pharmacology, Biochemistry and Behavior (2002), 73(2), 419-427
CODEN: PBBHAU; ISSN: 0091-3057

PB Elsevier Science Inc.

DT Journal

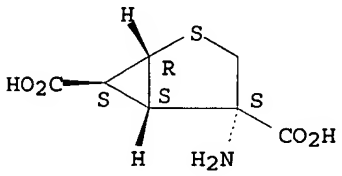
LA English

AB The involvement of Group II metabotropic receptors in acute and persistent pain states was evaluated in several in vivo models of pain with selective and potent Group II metabotropic glutamate (mGlu) 2,3 agonists. LY354740, LY379268 and LY389795 attenuated late-phase paw-licking pain behavior in a dose-dependent manner in the formalin model of persistent pain. Effects occurred in the absence of overt neuromuscular deficits as measured by performance in the rotorod test for ataxia. The effects of LY354740 and LY379268 were also stereoselective. The order of potency of the agonists was LY389795>LY379268>LY354740. The attenuation of licking behavior by LY379268 (3 mg/kg) in the formalin model was reversed by a potent and selective mGlu2,3 receptor antagonist, LY341495 (1 mg/kg). In the L5/L6 spinal nerve ligation model of neuropathic pain in rats, LY379268 significantly reversed mech. allodynia behavior in a dose-related manner. In contrast, LY379268 had no significant effects on the tail flick test or paw withdrawal test of acute thermal nociceptive function. These results support the involvement of Group II mGlu2,3 receptors in persistent pain mechanisms and suggest the potential utility of selective Group II mGlu agonists for the treatment of persistent pain.

IT **222529-89-7**, LY389795
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(group II mGluR receptor agonists are effective in persistent and

neuropathic pain models in rats)
RN 222529-89-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **222529-89-7**, LY389795
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(group II mGluR receptor agonists are effective in persistent and neuropathic pain models in rats)
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

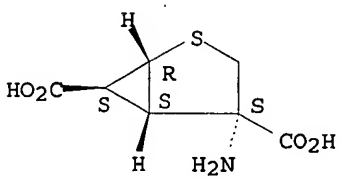
L19 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:741905 HCAPLUS
DN 133:305610
TI Treatment of neurological disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators
IN O'Neill, Michael John
PA **Eli Lilly** and Company Limited, UK
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO2000061126	A2	20001019	2000WO-GB01284	20000406
WO2000061126	A3	20010823		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI 1999GB-0008175 A 19990409
AB The present invention relates to a method of treating a neurol. disorder comprising administering to a patient an effective amount of a nitric oxide synthase inhibitor in combination with an effective amount of an excitatory amino receptor modulator. Combination of 2.5 mg/kg Mk-801, i.p., and 25 mg/kg ARL17477, i.p., had a synergistic degree of neuroprotection (78%) in cerebral ischemia induced in gerbils.
IT **222529-89-7**, LY 389795
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)
RN 222529-89-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-(9CI) (CA INDEX NAME)

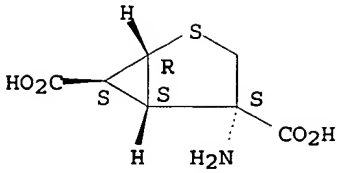
Absolute stereochemistry. Rotation (-).



IT **222529-89-7**, LY 389795
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

L19 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:74530 HCAPLUS
DN 132:217391
TI Neuroprotective actions of novel and potent ligands of group I and group II metabotropic glutamate receptors
AU Kingston, A. E.; O'Neill, M. J.; Bond, A.; Bruno, V.; Battaglia, G.; Nicoletti, F.; Harris, J. R.; Clark, B. P.; **Monn, J. A.**; Lodge, D.; Schoepp, D. D.
CS **Eli Lilly** and Co. Ltd., Windlesham, Surrey, GU20 6PH, UK
SO Annals of the New York Academy of Sciences (1999), 890(Neuroprotective Agents), 438-449
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
AB The role of group I metabotropic glutamate (mGlu) receptors in neurodegeneration is controversial because of the contradictory effects of mGlu1/5 agonists in in vitro models of neuronal cell death. In this study, novel and selective antagonists of mGlu1 and mGlu5: LY367385 and LY367366 were found to show consistent neuroprotective effects against N-methyl-D-aspartate (NMDA)-induced excitotoxicity in vitro and in vivo. Furthermore, intraventricular administration of LY367385 reduced hippocampal cell death in gerbils subjected to transient global ischemia. Previous studies have also shown that activation of group II mGlu receptors may contribute to neuroprotective mechanisms in vitro and in vivo. Three potent group II mGlu agonists-LY354740, LY379268 and LY389795-were found to attenuate both NMDA excitotoxicity and staurosporine-induced neuronal cell death. LY354740 and LY379268 were protective against transient global ischemia in gerbils when dosed i.p. These results support the view that antagonists of mGlu1 and mGlu5 and agonists of group II mGlu receptors may be useful agents in the therapeutic treatment of neurodegenerative disease.
IT **222529-89-7**, LY 389795
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective actions of novel and potent ligands of group I and group II metabotropic glutamate receptors)
RN 222529-89-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-(9CI) (CA INDEX NAME)

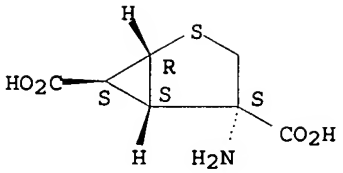
Absolute stereochemistry. Rotation (-).



IT **222529-89-7**, LY 389795
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective actions of novel and potent ligands of group I and group II metabotropic glutamate receptors)
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:546800 HCAPLUS
DN 131:281408
TI Neuroprotection by metabotropic glutamate receptor agonists: LY354740, LY379268 and LY389795
AU Kingston, Ann E.; O'Neill, Michael J.; Lam, Amy; Bales, Kelly R.; **Monn, James A.**; Schoepp, Darryle D.
CS **Eli Lilly, Lilly** Research Centre, Windleshanz, Surrey, GU20 6PH, UK
SO European Journal of Pharmacology (1999), 377(2/3), 155-165
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB In rat cortical neuronal cultures, metabotropic glutamate (mGlu) receptor agonists: LY354740 (+)-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylate; LY379268 (-)-2-oxa-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate, and LY389795 (-)-2-thia-4-aminobicyclo[3.1.0]- hexane-4,6-dicarboxylate, were neuroprotective against toxicity induced by N-methyl-D-aspartic acid (NMDA), kainic acid and staurosporine as measured by release of lactate dehydrogenase (LDH) activity into culture supernatants and DNA fragmentation by oligonucleosome formation. The potencies of the agonists were at least 100 times greater in reducing nucleosome formation than LDH release indicating a differential effect on neurons dying by apoptosis than by necrosis. In vivo studies showed that LY354740 was able to mediate a partial protection against apoptosis in CA1 hippocampal cells under ischemic conditions where substantial CAI cell loss occurred. The effects of the agonists in vitro were: (a) reversed by mGlu receptor antagonist LY341495, (b) enhanced by the presence of glial cells, (c) abrogated by RNA and protein synthesis inhibitors, and (d) unaltered by inhibition of endogenous adenosine activity. These results suggest that group 11 mGlu receptor agonists may represent a novel therapeutic strategy for the treatment of neurodegenerative diseases.
IT **222529-89-7**, LY 389795
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotection by metabotropic glutamate receptor agonists LY354740, LY379268 and LY389795)
RN 222529-89-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **222529-89-7**, LY 389795
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotection by metabotropic glutamate receptor agonists LY354740, LY379268 and LY389795)
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:137687 HCAPLUS
DN 130:282320
TI Synthesis, Pharmacological Characterization, and Molecular Modeling of Heterobicyclic Amino Acids Related to (+)-2-Aminobicyclo[3.1.0]hexane-2,6-dicarboxylic Acid (LY354740): Identification of Two New Potent, Selective, and Systemically Active Agonists for Group II Metabotropic Glutamate Receptors
AU **Monn, James A.**; Valli, Matthew J.; Massey, Steven M.; Hansen, Marvin M.; Kress, Thomas J.; Wepsiec, James P.; Harkness, Allen R.; Grutsch, John L., Jr.; Wright, Rebecca A.; Johnson, Bryan G.; Andis, Sherri L.; Kingston, Ann; Tomlinson, Rosemarie; Lewis, Richard; Griffey, Kelly R.; Tizzano, Joseph P.; Schoepp, Darryle D.
CS Discovery Chemistry Process Research and Development Neuroscience and Toxicology Research Divisions, **Eli Lilly** and Company, Indianapolis, IN, 46285, USA
SO Journal of Medicinal Chemistry (1999), 42(6), 1027-1040
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB As part of an ongoing research program aimed at the identification of highly potent, selective, and systemically active agonists for group II metabotropic glutamate (mGlu) receptors, novel heterobicyclic amino acids (-)-2-oxa-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate (LY379268, I) and (-)-2-thia-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate (LY389795, II) have been prepared. I and II are structurally related to the previously described nanomolar potency group II mGlu receptor agonist, (+)-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylate monohydrate (LY354740 monohydrate, III), with the C(4)-methylene unit of III being replaced with either an oxygen atom or a sulfur atom. I and II potently and stereospecifically displaced specific binding of the mGlu2/3 receptor antagonist ([3H]LY341495) in rat cerebral cortical homogenates, displaying IC50 values of 15 ± 4 and 8.4 ± 0.8 nM, resp., while having no effect up to 100,000 nM on radioligand binding to the glutamate recognition site on NMDA, AMPA, or kainate receptors. I and II also potently displaced [3H]LY341495 binding from membranes expressing recombinant human group II mGlu receptor subtypes: I Ki = 14.1 ± 1.4 nM at mGlu2 and 5.8 ± 0.64 nM at mGlu3; II Ki = 40.6 ± 3.7 nM at mGlu2 and 4.7 ± 1.2 nM at mGlu3. Evaluation of the functional effects of I and II on second-messenger responses in nonneuronal cells expressing human mGlu receptor subtypes demonstrated each to be a highly potent agonist for group II mGlu receptors: I EC50 = 2.69 ± 0.26 nM at mGlu2 and 4.58 ± 0.04 nM at mGlu3; II EC50 = 3.91 ± 0.81 nM at mGlu2 and 7.63 ± 2.08 nM at mGlu3. In contrast, neither compound (up to 10,000 nM) displayed either agonist or antagonist activity in cells expressing recombinant human mGlu1a, mGlu5a, mGlu4a, or mGlu7a receptors. The agonist effects of

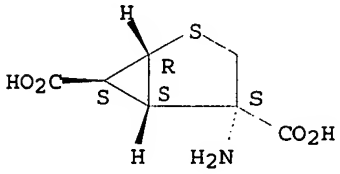
I and II at group II mGlu receptors were not totally specific, however, as mGlu6 agonist activity was observed at high nanomolar concns. for I (EC50 = 401 ± 46 nM) and at micromolar concns. (EC50 = 2 430 ± 600 nM) for II; furthermore, each activated mGlu8 receptors at micromolar concns. (EC50 = 1 690 ± 130 and 7 340 ± 2 720 nM, resp.). I.p. administration of either I or II in the mouse resulted in a dose-related blockade of limbic seizure activity produced by the nonselective group I/group II mGluR agonist (1S,3R)-ACPD (I ED50 = 19 mg/kg, II ED50 = 14 mg/kg), indicating that these mols. effectively cross the blood-brain barrier following systemic administration and suppress group I mGluR-mediated limbic excitation. Thus, I and II are novel pharmacol. tools useful for exploring the functions of mGlu receptors in vitro and in vivo.

IT **191471-53-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of aminooxa- and -thiabicyclohexanedicarboxylates as group II metabotropic glutamate receptor agonists)

RN 191471-53-1 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **191471-53-1P 222529-89-7P 222529-90-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of aminooxa- and -thiabicyclohexanedicarboxylates as group II metabotropic glutamate receptor agonists)

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:527203 HCAPLUS
DN 129:156945
TI Treatment for premenstrual dysphoric disorder
IN Levine, Louise R.
PA **Eli Lilly** and Company, USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO---9832436	A1	19980730	1998WO-US01344	19980123
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA---2275777	A1	19980730	1998CA-2275777	19980123

	AU---9862487	A	19980818	1998AU-0062487	19980123
	EP---1014971	A1	20000705	1998EP-0904669	19980123
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
	JP2001511131	T	20010807	1998JP-0532158	19980123
PRAI	1997US-036176P	P	19970129		
	1998WO-US01344	W	19980123		

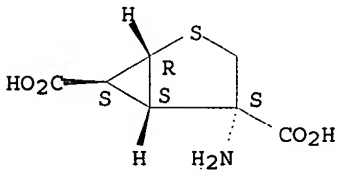
AB Agonists which act at neg.-coupled cAMP-linked metabotropic glutamate receptors are useful for treating premenstrual dysphoric disorder. An example compound which was synthesized is 1SR,4SR,5SR,6SR-4-amino-2-oxabicyclo[3.1.0]hexane-4,6-dicarboxylic acid.

IT **191471-53-1P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oxa- and thiabicyclohexanedicarboxylates for treatment of premenstrual dysphoric disorder)

RN 191471-53-1 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **191471-53-1P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oxa- and thiabicyclohexanedicarboxylates for treatment of premenstrual dysphoric disorder)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 1997:752747 HCAPLUS

DN 127:359103

TI Preparation of bicyclic excitatory amino acid derivatives

IN Massey, Steven Marc; **Monn, James Allen**; Valli, Matthew John

PA **Eli Lilly** and Co., USA

SO U.S., 15 pp.
CODEN: USXXAM

DT Patent

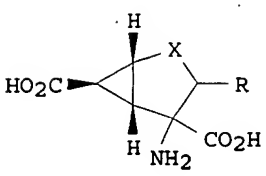
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US---5688826	A	19971118	1996US-0749140	19961114
PRAI	1996US-0749140		19961114		

OS MARPAT 127:359103

GI



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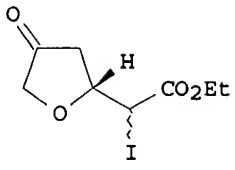

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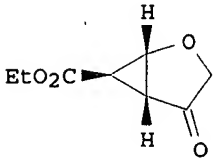

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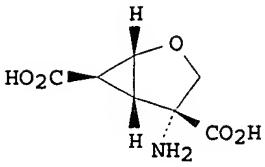


IV

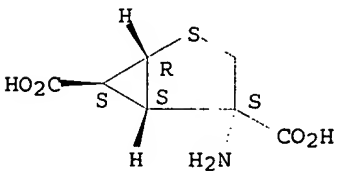
AB Title compds. I [X = O, NR1, S, S(O), SO2; R = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, (un)substituted aromatic group, (un)substituted heteroarom. group, non-aromatic carbocyclic group, non-aromatic heterocyclic group, non-aromatic monocyclic carbocyclic group fused with 1-2 monocyclic aromatic or heteroarom. groups, non-aromatic monocyclic heterocyclic group fused with 1-2 monocyclic aromatic or heteroarom. groups, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl substituted by 0-3 (un)substituted aromatic groups, (un)substituted heteroarom. groups, non-aromatic carbocyclic groups, non-aromatic heterocyclic groups, non-aromatic monocyclic carbocyclic group fused with 1-2 monocyclic aromatic or heteroarom. groups, non-aromatic monocyclic heterocyclic group fused with 1-2 two monocyclic aromatic or heteroarom. groups; R1 = H, (CO)nR; n = 0-1], non-toxic metabolically labile esters or amides thereof, and pharmaceutically acceptable salts thereof are useful as modulators of metabotropic glutamate receptor function. Thus, selective ketalization of (S)-(-)-1,2,4-butanetriol with acetone, followed by oxidation, Wittig olefination with (carbethoxymethylene)triphenylphosphorane, deprotection, iodolactonization, and oxidation gave tetrahydrofuranylacetate II. Treatment of II with DBU in EtOAc gave oxabicyclo[3.1.0]hexanonecarboxylate III, which was converted into title compound IV via spirohydantoin formation with (NH4)2CO3 and KCN, followed by basic hydrolysis and saponification formulations containing I are also given.

IT **191471-53-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bicyclic excitatory amino acid derivs.)

RN 191471-53-1 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



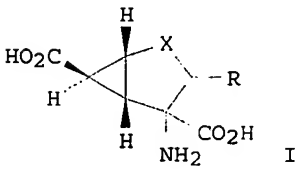
IT **191471-53-1P 191471-54-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of bicyclic excitatory amino acid derivs.)

L19 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:443241 HCAPLUS
DN 127:66216
TI Preparation of excitatory amino acid derivatives
IN **Monn, James Allen**; Valli, Matthew John; Massey, Steven Marc
PA **Eli Lilly** and Co., USA
SO Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP----774461	A1	19970521	1996EP-0308216	19961114
	EP----774461	B1	20060308		
	R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CA---2237910	A1	19970522	1996CA-2237910	19961112
	CA---2237910	C	20051227		
	WO---9718199	A1	19970522	1996WO-US18112	19961112
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
	RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU---9677279	A	19970605	1996AU-0077279	19961112
	AU----703409	B2	19990325		
	ZA---9609486	A	19980512	1996ZA-0009486	19961112
	CN---1202167	A	19981216	1996CN-0198396	19961112
	BR---9611511	A	19990504	1996BR-0011511	19961112
	JP2000500748	T	20000125	1997JP-0518993	19961112
	IL----124487	A	20010111	1996IL-0124487	19961112
	HU---9903459	A2	20010428	1999HU-0003459	19961112
	HU---9903459	A3	20010828		
	TW----422836	B	20010221	TW 1996-85113881	19961113
	AT----319685	T	20060315	1996AT-0308216	19961114
	ES---2258771	T3	20060901	1996ES-0308216	19961114
	NO---9802202	A	19980514	1998NO-0002202	19980514
PRAI	1995US-006864P	P	19951116		
	1996GB-0005434	A	19960315		
	1996WO-US18112	W	19961112		

OS MARPAT 127:66216
GI



I

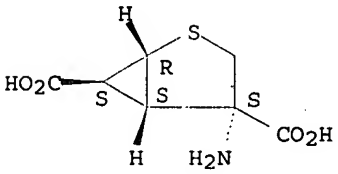
AB Bicyclic amino acids I [X = O, NH, NR, NCOR, S, SO, SO2; R = H or (un)substituted alkyl, alkenyl, alkynyl, aryl, carbocyclyl, heterocyclyl] or their pharmaceutically acceptable salts were prepared for use as modulators of metabotropic glutamate receptor function. Thus, 1SR,4SR,5RS,6SR-4-amino-2-oxabicyclo[3.1.0]hexane-4,6-dicarboxylic acid was prepared in several steps from 1,2,4-butanetriol and (carbethoxymethylene)triphenylphosphorane. Formulations containing I are described.

IT **191471-53-1P**

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(excitatory amino acid derivs.)

RN 191471-53-1 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



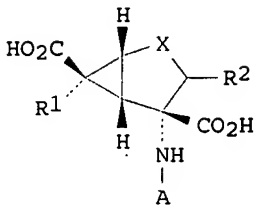
IT **191471-53-1P 191471-54-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(excitatory amino acid derivs.)

=> d bib abs hitstr 132

L32 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:991499 HCAPLUS
DN 140:42463
TI Preparation of prodrugs of excitatory amino acids
IN Moher, Eric David; Monn, James Allen; Pedregal-Tercero, Concepcion
PA Eli Lilly and Company, USA; Collado, Cano Ivan; Blanco-Urgoiti, Jamie Gonzalo
SO PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2003104217	A2	20031218	2003WO-US15405	20030606
	WO2003104217	A3	20040226		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA---2488167	A1	20031218	2003CA-2488167	20030606
	AU2003232146	A1	20031222	2003AU-0232146	20030606
	EP---1517915	A2	20050330	2003EP-0757266	20030606
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP2006503807	T	20060202	2004JP-0511287	20030606
	US2005222231	A1	20051006	2004US-0516559	20041130
	IN2004KN01838	A	20060721	2004IN-KN01838	20041202
	NO2005000122	A	20050110	2005NO-0000122	20050110
PRAI	2002EP-0380120	A	20020611		
	2002EP-0380121	A	20020611		
	2002US-415936P	P	20021003		
	2002US-415937P	P	20021003		
	2003WO-US15405	W	20030606		

OS MARPAT 140:42463
GI



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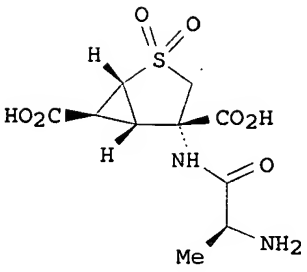


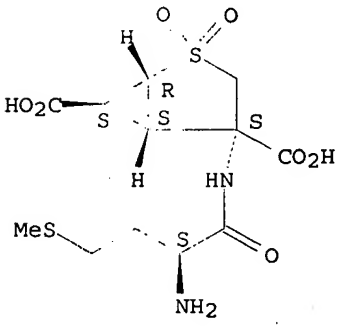
II

AB The invention relates to synthetic excitatory amino acid prodrugs for the treatment of neurol. disorders and psychiatric disorders. Bicyclic amino acids I [A is H-Q1-10, where Q is aminoacyl; X is O, S, SO, SO2, or substituted methylene; R1 is H or F; R2 is H, F, or OH] or their pharmaceutically-acceptable salts are claimed. Thus, prodrug II.HCl was prepared via peptide coupling reaction and shown to exhibit comparable concentration in rat plasma to that of the non-prodrug form.

IT **635318-26-2P 635318-55-7P 635318-56-8P**
635318-57-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of excitatory amino acids)

RN 635318-26-2 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-4-(methylthio)-1-oxobutyl]amino]-, 2,2-dioxide, monohydrochloride, (1R,4S,5S,6S)- (9CI) (CA INDEX NAME)

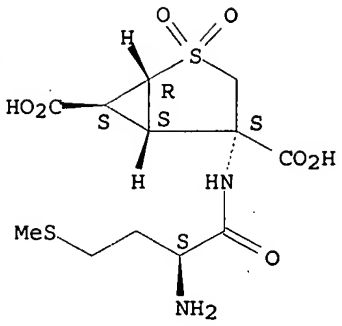
Absolute stereochemistry. Rotation (+).



● HCl

RN 635318-55-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-4-(methylthio)-1-oxobutyl]amino]-, 2,2-dioxide, (1R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

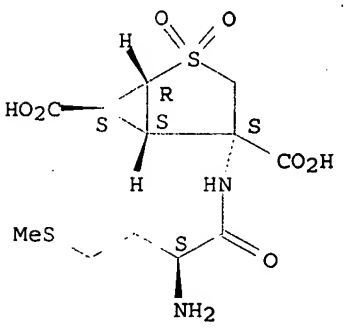


RN 635318-56-8 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-4-(methylthio)-1-oxobutyl]amino]-, 2,2-dioxide, (1R,4S,5S,6S)-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

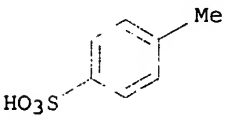
CRN 635318-55-7
CMF C12 H18 N2 O7 S2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 104-15-4
CMF C7 H8 O3 S

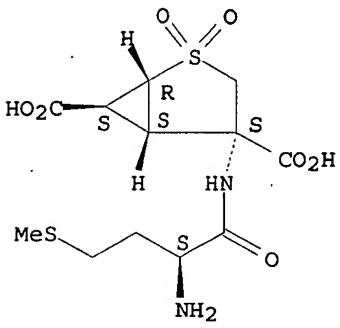


RN 635318-57-9 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-4-(methylthio)-1-oxobutyl]amino]-, 2,2-dioxide, (1R,4S,5S,6S)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

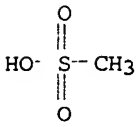
CRN 635318-55-7
CMF C12 H18 N2 O7 S2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S



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L29 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
AN **2003:818322** HCAPLUS
DN 139:302068
TI Therapy for psychoses combining an atypical antipsychotic and an mGlu2/3 receptor agonist
IN Johnson, Bryan Glenn; Schoepp, Darryle Darwin
PA **Eli Lilly** and Company, USA
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2003084610	A1	20031016	2003WO-US07283	20030321
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA---2478227	A1	20031016	2003CA-2478227	20030321
	AU2003218063	A1	20031020	2003AU-0218063	20030321
	EP---1492595	A1	20050105	2003EP-0714045	20030321
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

	JP2005528378	T	20050922	2003JP-0581846	20030321
	US2005192273	A1	20050901	2004US-0509772	20040928
PRAI	2002US-369771P	P	20020403		
	2002US-369797P	P	20020403		
	2003WO-US07283	W	20030321		

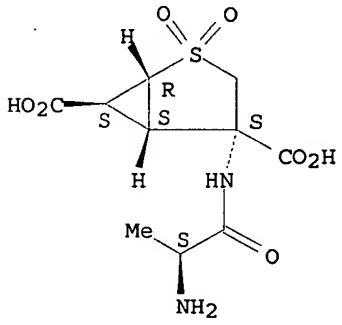
AB The invention provides a pharmaceutical composition and methods for treating psychosis comprising the combination or a first component which is an atypical antipsychotic with a second component which is a mGlu2/3 receptor agonist. The invention also provides a pharmaceutical composition and method of treating a psychiatric disorder comprising the combination of a first component which is an atypical antipsychotic with a second component which is a compound which allosterically enhances receptor activity for mGlu2 and/or mGlu3.

IT **611168-14-0**, LY 404039
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(atypical antipsychotic-mGlu2/3 receptor agonist combination for treatment of psychoses and psychiatric disorders)

RN 611168-14-0 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-1-oxopropyl]amino]-, 2,2-dioxide, (1R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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http://www.stn-international.de/archive/stn_online_news/fraghitstr_ex.pdf

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PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
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http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX
PLEASE SEE
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<
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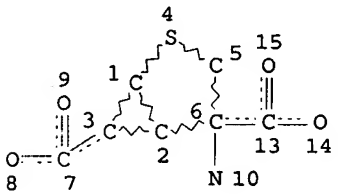
=> d que sta l43
L7 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 5 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

=> d max l46

L46 ANSWER 1 OF 1 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
AN 2004-098898 [10] WPIX
ED 20050528
DNC C2004-040767 [10]
TI New amino acid prodrugs useful for treating e.g. psychiatric disorder and neurological disorder e.g. Tourette's syndrome, tardive dyskinesia, schizophrenia and anxiety
DC B03; B05; P34
IN BLANCO-URGOITI J G; BROOME T E; LADUCA P; MOHER E D; MONN J A; PEDREGAL-TERCERO C; SALAHIEH A; SCHULTZ M; BLANCO-URGIOTI J G; COLLADO CANO I
PA (BROO-I) BROOME T E; (LADU-I) LADUCA P; (ELIL-C) LILLY & CO ELI; (SALA-I) SALAHIEH A; (SCHU-I) SCHULTZ M
CYC 103
PI WO--2003104217 A2 20031218 (200410)* EN 172[0]
US-20040127936 A1 20040701 (200444) EN
AU--2003232146 A1 20031222 (200445) EN
EP-----1517915 A2 20050330 (200522) EN
NO---200500122 A 20050110 (200523) NO C07K-005/06
KR--2005009742 A 20050125 (200535) KO C07D-333/78
US-20050222231 A1 20051006 (200566) EN

TW---200400815 A 20040116 (200567) ZH A61K-031/195
MX--2004012518 A1 20050301 (200568) ES
JP--2006503807 W 20060202 (200611) JA 115
IN---200401838 P2 20060721 (200656) EN
ZA---200409553 A 20060927 (200669) EN 183 C07K-000/00

ADT WO--2003104217 A2 2003WO-US0015405 20030606; US-20040127936 A1 Provisional 2002US-000415936P 20021003; US-20050222231 A1 Provisional 2002US-000415936P 20021003; US-20050222231 A1 Provisional 2002US-000415937P 20021003; TW---200400815 A 2003TW-000114268 20030527; AU--2003232146 A1 2003AU-000232146 20030606; EP-----1517915 A2 2003EP-000757266 20030606; EP-----1517915 A2 2003WO-US0015405 20030606; NO---200500122 A 2003WO-US0015405 20030606; US-20050222231 A1 2003WO-US0015405 20030606; MX--2004012518 A1 2003WO-US0015405 20030606; JP--2006503807 W 2003WO-US0015405 20030606; IN---200401838 P2 2003WO-US0015405 20030606; US-20040127936 A1 2003US-000677716 20031002; JP--2006503807 W 2004JP-000511287 20030606; US-20050222231 A1 2004US-000516559 20041130; IN---200401838 P2 2004IN-KOLNP1838 20041202; KR--2005009742 A 2004KR-000720013 20041209; MX--2004012518 A1 2004MX-000012518 20041210; NO---200500122 A 2005NO-000000122 20050110; ZA---200409553 A 2004ZA-000009553 20041125

FDT AU--2003232146 A1 Based on WO--2003104217 A; EP-----1517915 A2 Based on WO--2003104217 A; MX--2004012518 A1 Based on WO--2003104217 A; JP--2006503807 W Based on WO--2003104217 A

PRAI 2002US-000415937P 20021003
2002EP-000380120 20020611
2002EP-000380121 20020611
2002US-000415936P 20021003
2003US-000677716 20031002

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ICS A61K-07K/; C07C-229/00; C07D-333/48

IPCI A61K-0038/00 [I,A]; A61P-0001/00 [I,C]; A61P-0001/08 [I,A]; A61P-0013/00 [I,C]; A61P-0013/02 [I,A]; A61P-0019/00 [I,A]; A61P-0021/00 [I,A]; A61P-0021/04 [I,A]; A61P-0025/00 [I,A]; A61P-0025/06 [I,A]; A61P-0025/08 [I,A]; A61P-0025/14 [I,A]; A61P-0025/16 [I,A]; A61P-0025/18 [I,A]; A61P-0025/20 [I,A]; A61P-0025/22 [I,A]; A61P-0025/24 [I,A]; A61P-0025/28 [I,A]; A61P-0025/30 [I,A]; A61P-0025/34 [I,A]; A61P-0027/00 [I,C]; A61P-0027/02 [I,A]; A61P-0029/00 [I,A]; A61P-0003/00 [I,C]; A61P-0003/10 [I,A]; A61P-0031/00 [I,C]; A61P-0031/18 [I,A]; A61P-0043/00 [I,A]; A61P-0009/00 [I,C]; A61P-0009/10 [I,A]; C07K-0005/00 [I,C]; C07K-0005/06 [I,A]

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AB WO 2003104217 A2 UPAB: 20060121

NOVELTY - Amino acid prodrugs or their salts are new.

DETAILED DESCRIPTION - Amino acid prodrugs of formula (I) or its salts are new.

A = H-(Q)p-;

Q = amino acyl;

p = 1 - 10;

X = O, S, SO, SO2 or CR3R4;

R3 = F, X'OR5, SO3H, tetrazol-5-yl, CN, PO3(R6)2, OH, NO2, N3, (CH2)mCOOR5a, (CH2)mPO3(R6a)2, NHCONHR5b, NHSO2R5c, amino or carboxyl;

R4 = H, F, amino or carboxyl;

R3+R4 = =O, =NOR7, =CR8R9, =CHCOOR5b, =CHPO3(R6a)2, or =CHCN;

X' = a bond, CH2 or CO;

m = 1 - 3;

R5, R5a, R5b, R5c and R7 - R9 = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, aromatic group, or heteroaromatic group (all optionally substituted), H, non-aromatic carbocyclic group, non-aromatic heterocyclic group, non-aromatic monocyclic carbocyclic group or non-aromatic monocyclic heterocyclic group (both fused with at least one monocyclic aromatic or heteroaromatic groups);

R6 and R6a = H or 1-6C alkyl;
R10 = H or F; and
R11 = H, F or OH.
One of R3 or R4 is amino and the other is carboxyl.
An INDEPENDENT CLAIM is included for the preparation of (I).
ACTIVITY - Neuroprotective; Cardiant; Vasotropic; Vulnerary; Cerebroprotective; Tranquilizer; Immunosuppressive; Nootropic; Anticonvulsant; Anti-HIV; Respiratory-Gen.; Antidiabetic; Ophthalmological; Antiparkinsonian; Antimigraine; Analgesic; Uropathic; Antiaddictive; Antismoking; Antiemetic; Antiinflammatory; Hypnotic; Neuroleptic; Muscular-Gen.; Antidepressant.
MECHANISM OF ACTION - mGluR2 receptor agonist. The ability of (I) to determine the mGluR2 receptor agonist activity was determined using CHO cells over-expressing the hPepT1 transporter and the EC50 value was found to be less than 5 mM. No specific results for specific compounds given.
USE - For affecting the cAMP-linked metabotropic glutamate receptor for modulated excitatory amino acid neurotransmission; and for treating neurological disorder (e.g. cerebral deficits subsequent to cardiac bypass and grafting, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, perinatal hypoxia, hypoglycemic neuronal damage, ocular damage and retinopathy, cognitive disorders, idiopathic and drug-induced Parkinson's Disease, muscular spasms, migraine headaches, urinary incontinence, drug tolerance, withdrawal, cessation, and craving, smoking cessation, emesis, brain edema, chronic pain, sleep disorders, convulsions, Tourette's syndrome, attention deficit disorder, and tardive dyskinesia) and psychiatric disorder (e.g. schizophrenia, anxiety and related disorders, depression, bipolar disorders, psychosis, and obsessive compulsive disorders) (all claimed).
ADVANTAGE - The compound maintains the safety and efficacy of prior art compound with increased oral bioavailability.

TECH ORGANIC CHEMISTRY - Preparation (claimed): Preparation of (I) involves: acylating a protected amino acid compounds of formula (i) with a amino acyl of formula PgN-A (ii). The protecting group is removed, when functional group is protected using a protecting group. The method optionally further involves either:
(1) reacting the basic form of (I) with an acid having a counterion;
(2) for (I) (having an acidic moiety), reacting the acidic form of (I) with a base having a cation; or
(3) for (I) (zwitterionic compound), neutralizing the acid-addition salt form or base-addition salt of (I).
Pgc = protecting group; and
PgN = nitrogen-protecting group.

ABEX DEFINITIONS - Preferred Definitions: - Q = L-alanyl; - p = 1; - X = SO2 or CR3R4; - R3 = F; - R4, R10 and R11 = H; and - R3+R4 = =O.
ADMINISTRATION - The dosage is 25 - 300 mg and administered orally.
SPECIFIC COMPOUNDS - 14 Compounds are specifically claimed as (I), e.g. (1R,4S,5S,6S)-4-(2'S-aminopropionyl)amino)-2,2-dioxo-2lambda6-thia-bicyclo(3.1.0)hexane-4,6-dicarboxylic acid hydrochloride.
EXAMPLE - To a suspension of (1R,4S,5S,6S)-4-(2'S-tert-butoxycarbonylaminopropionylamino)-2,2-dioxo-2lambda6-thia-bicyclo(3.1.0)hexane-4,6-dicarboxylic acid (110 g) in ethyl acetate (563 ml) was added a solution of hydrogen chloride in ethyl acetate (514 ml) over 20 minutes. After work up (1R,4S,5S,6S)-4-(2'S-aminopropionyl)amino)-2,2-dioxo-2lambda6-thia-bicyclo(3.1.0)hexane-4,6-dicarboxylic acid. hydrochloride (85.77 g; yield 92%) was obtained.

IT UPIT 20060121
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FS CPI; GMPI

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FILE LAST UPDATED ON JANUARY 10, 2007

FILE COVERS 1771 TO 2006.
*** FILE CONTAINS 9,780,003 SUBSTANCES ***

>>>PLEASE NOTE: Reaction Data and substance data are stored in
separate documents and can not be searched together in one query.
Reaction data for BEILSTEIN compounds may be displayed
immediately with the display codes PRE (preparations) and REA
(reactions). A substance answer set retrieved after the search
for a chemical name, a compounds with available reaction

information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

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*** NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.**

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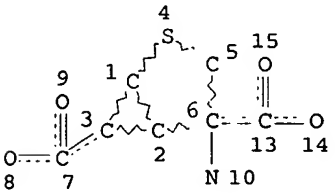

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE CONTENT: 1961-PRESENT VOL 146 ISS 12 (20070316/ED)

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MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 2007021624 25 JAN 2007
DE 102005037076 25 JAN 2007
EP 1746674 24 JAN 2007

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JP   2007019376 25 JAN 2007
WO   2007017126 15 FEB 2007
GB      2427406 27 DEC 2006
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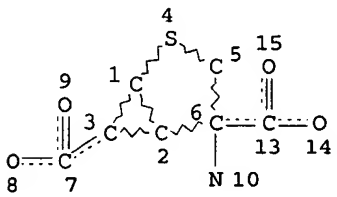


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L16            2 E4-5
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L18        15226 (ELI LILLY OR LILLY OR ELI)/PA,CS
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                 SEL AN L28 2
L29            1 E8-9 AND L28

     FILE 'REGISTRY' ENTERED AT 12:00:00 ON 22 MAR 2007
L30            3 E10-12
L31            4 L9 AND C12H18N2O7S2

     FILE 'HCAPLUS' ENTERED AT 13:08:17 ON 22 MAR 2007
L32            1 L31

     FILE 'HCAOLD' ENTERED AT 13:10:28 ON 22 MAR 2007
L33            0 L9

     FILE 'MEDLINE' ENTERED AT 13:10:34 ON 22 MAR 2007
L34            0 L9

     FILE 'BIOSIS' ENTERED AT 13:10:40 ON 22 MAR 2007
L35            7 L9
                 SEL HIT RN L35

     FILE 'REGISTRY' ENTERED AT 13:12:14 ON 22 MAR 2007
L36            1 E13

     FILE 'EMBASE' ENTERED AT 13:12:31 ON 22 MAR 2007
L37           16 L9
                 SEL HIT RN L37

     FILE 'REGISTRY' ENTERED AT 13:12:48 ON 22 MAR 2007
L38            1 E14

     FILE 'BEILSTEIN' ENTERED AT 13:13:34 ON 22 MAR 2007
L39            4 L7 FULL

     FILE 'MARPAT' ENTERED AT 13:14:34 ON 22 MAR 2007
L40            0 L7 SAM
L41            6 L7 FULL

     FILE 'WPIX' ENTERED AT 13:17:38 ON 22 MAR 2007
L42            1 L7
L43            4 L7 FULL
L44            3 L43 AND (835458-1-1-0 OR 835460-1-1-0 OR 835466-1-0-0)/DCSE
                 SEL DCSE
                 EDIT /DCSE /DCRE
L45            0 E15-17
```

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                SEL SDCN L44
                EDIT /SDCN /DCN
L46           1 E18-20

=>
```